Cellular Biophysics
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Random walk statistics, Stoke-Einstein
Part: 01

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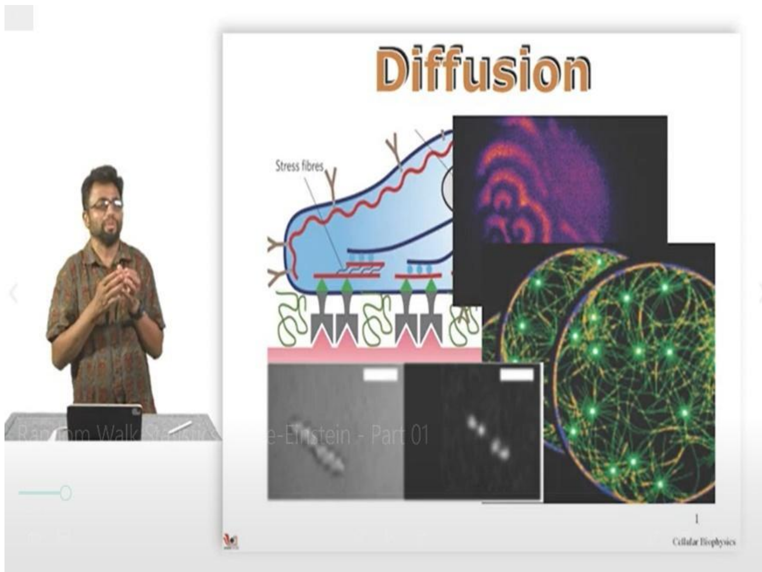

Hi welcome back today we are going to continue on a slightly different topic but one that I keep touching upon I have mentioned diffusion again and again today we are going to dive straight into the question of diffusion. I am going to talk to you a little bit in terms of a brief background and then we will dive into details of the physical theory of diffusion, how it relates to thermodynamics and how that connects to cell biology and quantitative biology which then becomes what we keep calling cellular biophysics.

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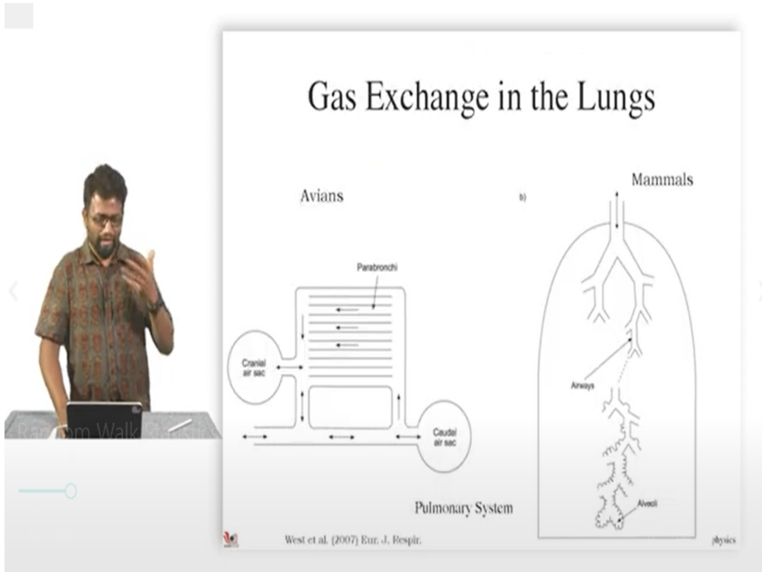

So we are kind of familiar with diffusion but you will be surprised to learn that it is critical for the thing that we do right now breathe. So some of you maybe practice yoga and some of you watch yoga on TV it is quite popular these days. This process of inhalation exhalation is driving air even while we while I talk into our lungs. The lungs are nothing but branched networks of cells of tissue with air gaps and at the smallest cavity of the air gaps there is diffusive exchange of gases in our lungs.

So in that sense understanding diffusion is not just something obscure and basic science and we do not care but something fundamental to life itself our life human life and we value human life and we value our good health and coronavirus is an aerially transmitted disease. So we wear masks normally because we want to protect our airways because this virus attacks our airways.

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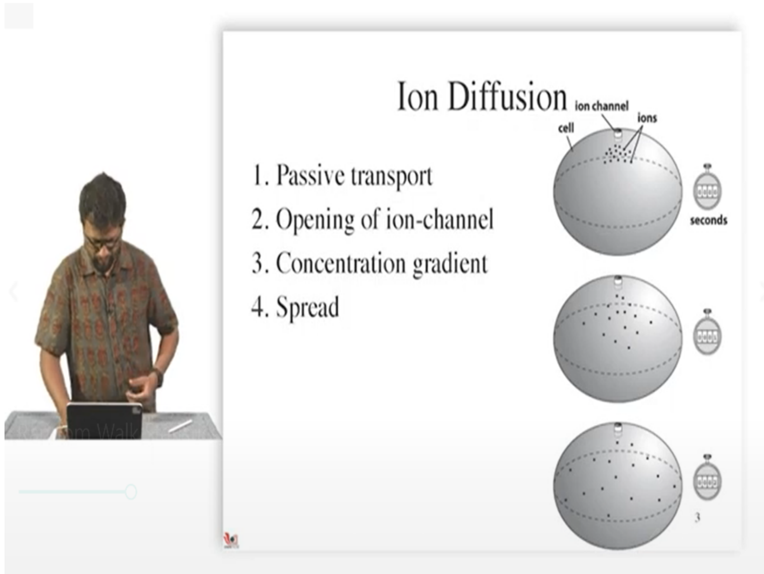

So another very common process in which diffusion is critical at a cellular scale is a neuronal system. And ion diffusion which both occurs through channels that are dedicated for the transport of ions those are ion channels. As well as passive transport through the membrane itself diffusion through the membrane both are responsible for controlling our neuronal activity.

So these are crucial factors and therefore understanding the physical basis of it because it is a physical process becomes critical. So in some senses passive transport is related to the process by which without channels also ions can move in. Opening and closing of ion channels can of course regulate their flow and concentration gradients are the key driver in diffusion of ions from inside to out or outside to in. But they are also responsible for the spread of ions because even when there is no concentration gradient ions are still going to be moving around and spreading uniformly.

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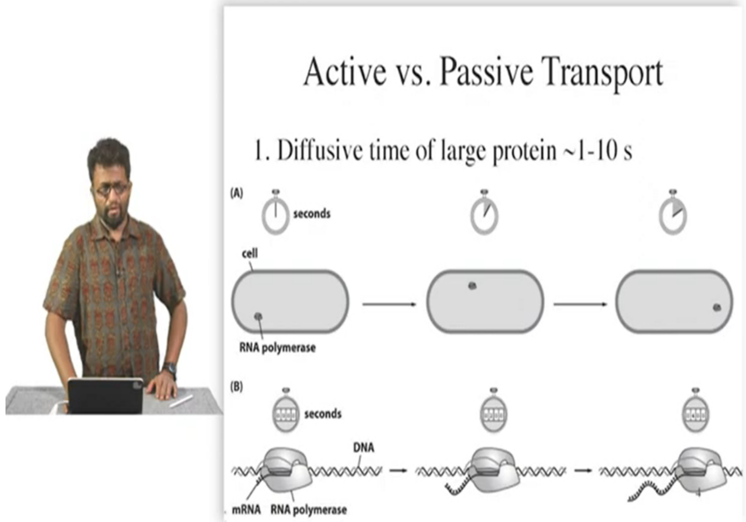

In a sense you could argue that diffusion forms the basis of transport at a cellular level and we are all familiar with those beautiful movies of molecular motors walking and we will have a chance to talk about them in the later segments of this course. But diffusion is an important and almost often ignored aspect in cell biology of how things move around.

So for example an RNA polymerase that is present in one part of the cell can move to the other parts within about 1 to 10 seconds purely by diffusion. Purely by the same random walk that we think particles of air that are around us that are performing I am sorry DNA on a poly with a polymerase that is transcribing it translocates in similar times but that is not passive transport we know that this is active transport. So we argue that active and passive transport diffusive transport have similar time scales.

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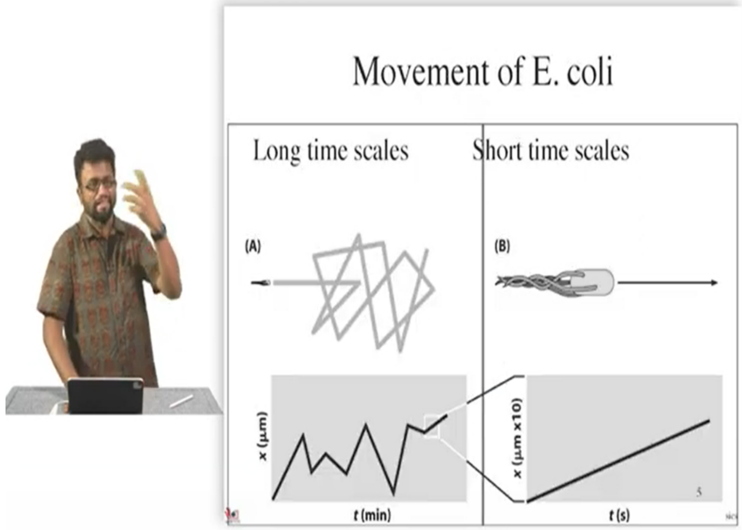

Longer time scales like seconds tens of seconds minutes we see directed motion and one of these classic examples is equalize motion. and if you remember in the Reynolds number segment we talked a lot about low Reynolds numbers, the rule of drag, the nature of random walk of e coli, the funny part is that e coli is small enough two microns in length one micron in diameter. That in fact it is subject to thermal motion and will undergo diffuse motion in short time scales but in long time scales it undergoes vectorial motion.

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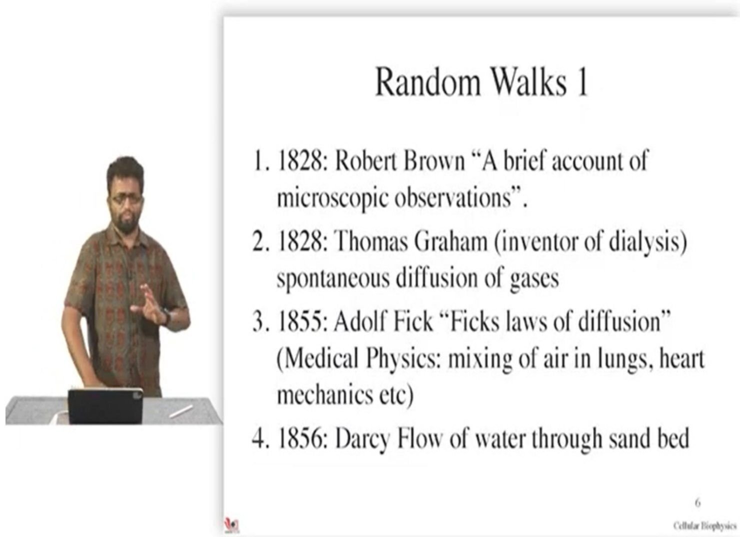

And so what a little bit of history of random walks is important here to highlight that Robert Brown made a series of microscopic observations and I think this is an important lesson. Because sometimes your curiosity to just know what is there is such an important driver in scientific discovery and you do not need to know too much history.

So sometimes I would suggest if you have a microscope please go to a pond or a little stream or if you live near the ocean then the river or in the well that you take your water from and look under the microscope just look. Because you will be fascinated I am fascinated every time I have the chance to do this and Robert Brown in 1828 was fascinated.

He wrote his observations in terms of a brief account of microscopic observations so this is the second part of scientific discovery by the way write down write down what you see. Try to explain maybe it is just for yourself maybe no teacher is going to look at it no professor has time to read your diary, but write it because you never know when you will be the new discoverer the new Brown. Thomas graham the also the inventor of dialysis discovered the spontaneous diffusion of gases the one that I was talking about in which is involved in the exchange of gases in your lung.

Adolf Fick who came up with fixed laws of deficient 1855 medical physics mixing of air in lungs, heart and mechanics is another pioneer in the theory of random walks. And Darcy in 1856 worked on the flow of water through sand bed. So these are some of the people who have been major contributors and unfortunately you see it is all 1800s.

So in some senses these are old theories but old theories that work this is not about history or geography or which country or something is just simply if you do the same experiments you will get the same answers and that is the beauty of science.

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But strangely you will be surprised to know that random walk and diffusion theory is also used in finance. So if you want to make a lot of money stock markets are your option Harshad Mehta number two. These transitions of the stock market prices I think I have taken them from yahoo finance some years ago this was 9 9 am on I think 2021, show these fluctuations which almost resemble stochastic fluctuations that come out of random walks. And random models have been very successful in explaining the kind of behavior that we see in these statistical data.

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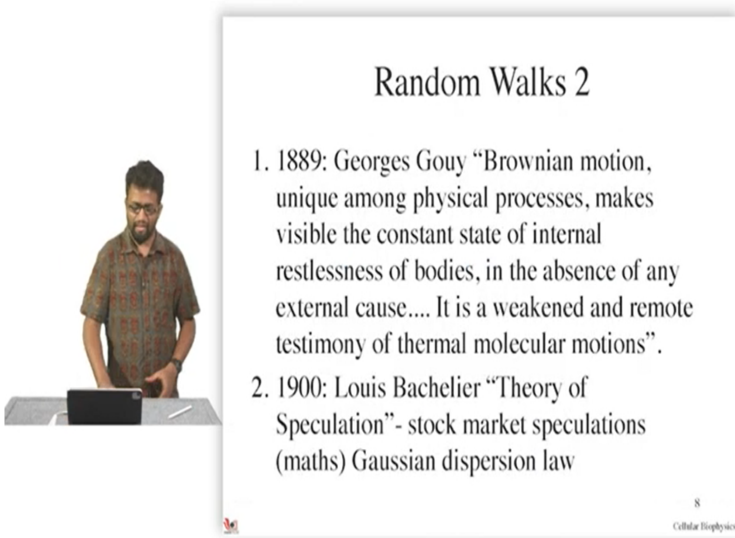

Indeed George Gouy said something very beautiful about random walks he said Brownian motion is unique amongst physical processes. Because it makes visible the constant state of internal restlessness of bodies in the absence of any external cause it is a weakened and remote testimony of thermal molecular motion.

This is such a eloquent sentence such a well written sentence because in fact it illustrates the fact that if you as I said take a microscope and look it does not matter whether animals or insects or no living things in it you will see motion. And this motion is not because you were thumping the table or your dog was coming around and barking at you it is just simply because of heat the ambient 30 degrees 40 degrees depending on the temperature in your in your town or city or your lab that is the cause of the motion.

And this is really because it is elegant because this pure energy it is around us everywhere. Now, so when I said random walks in finance Louis Bachelier in 1900s published his Phd thesis in mathematics it is called the theory of speculation I do not know the French words for it. This was indeed the first attempt at using the laws of random walks and division to mathematical prediction of stock market values. We do not know how successful he was financially but certainly he set the stage for a lot of what are called quants or quantitative mathematical approaches in mathematical finances.

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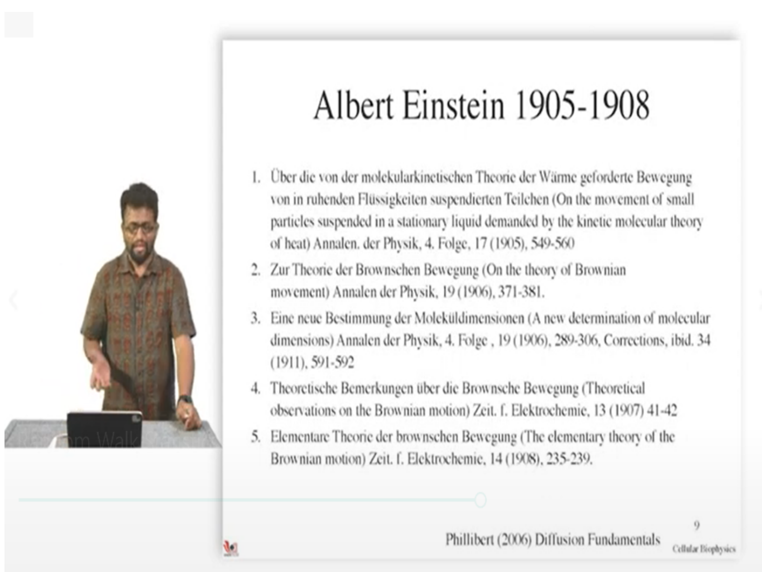

And we come to 1905 to 1908 so you remember my earlier description of luminaries of contributors to division and random walks were from the 1800s. Now we are 1905- 1908 and we come to albert Einstein, albert Einstein was as you know a Jewish researcher in Berlin he was made to leave or he was frightened of his life. So he left because there was political persecution in Germany. He went to Switzerland where he worked as a patent attorney and in that strange time he and his wife who was herself a mathematician they worked out a series of papers this is 1905 to 1908 period.

The first paper is translated as the about the molecular kinetic theory of heat and it is consequent motion in fluids that are at rest of suspended particles. In other words on the movement of suspended particles in a stationary liquid demanded by the kinetic theory of molecular or kinetic molecular theory of heat. This is published in a journal that you will never have heard of it is not nature science cell or fizz rev letters it is called annalen der physik. It does not exist anymore as far as I know in this in that old form because it was a German journal.

He then went on to write a paper on the theory of Brownian movement which is also annalen der physik 'Eine neue Bestimmung der Moleküldimensionen' a new dimension determination of molecular dimensions also in the same journal 1906. So you see this very productive time when he was working as a patent attorney and patent examiner in the Swiss patent office in Bern in Switzerland. Which means that you can do research excellent research groundbreaking research even if you do not have all the means to it of course theory is easy because you do not need a lab when you need a lab things are a bit trickier.

But remember that you have to look beyond your own limitations and we live in a country India we have high contrast sometimes we have very fancy labs sometimes we have no labs rather than complain about it try to find a way around it and hopefully you will get better.

The final paper in the series was elementary theory of Brownian motion which was published in 1908 in the side shift electrochemic journal for electrochemistry. My only point of bringing this up is the fact that these theories are more than 110 years 115 years old and they are still relevant and they make sense to us and they help us explain a lot of things.

And secondly that prominence of the journals where the work is published is not as important as the prominence of the work itself and it is what we refer to as the test of time. So if the work is valid then it will remain whether it is Archimedes whether it is Sushrut whether it is Albert Einstein.

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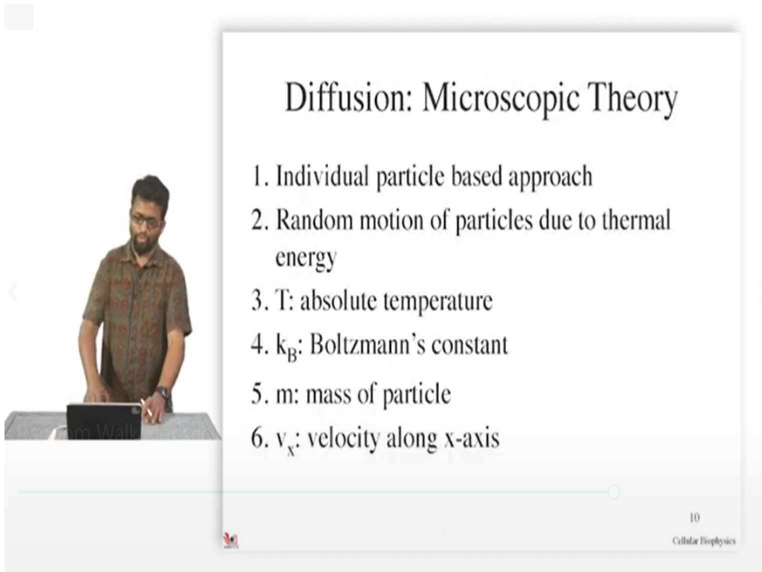

So we are interested in the macromolecule the microscopic theory that underlies diffusion. When we observe particles when Brown Robert brown observed particles moving around he knew that they were moving but he did not know why.

In fact the first idea was that they are alive so he went into coal particles he took a candle and make made a suit out of it took those suit particles suspended them in water looked into them under the microscope and he saw they were moving. So suit is not alive we know that but he said or maybe some insect got in the way. So he went to a friend who went to Egypt to the to the pyramids and he took a brick from the pyramids and crushed it of course that is four thousand five thousand years old.

That must not be alive now there must be nothing living in it and he looked under the microscope and it still moved so he said oh this is crazy something keeps moving even if it is dead for thousands of years how is that possible. And that how is that possible is in a way answered by Einstein's work because individual particles require to be thought of as individual particles random motion is due to thermal energy and this thermal energy is given by t which is the absolute temperature in kelvin and Kb which is Boltzmann's constant and mass of the particle and velocity.

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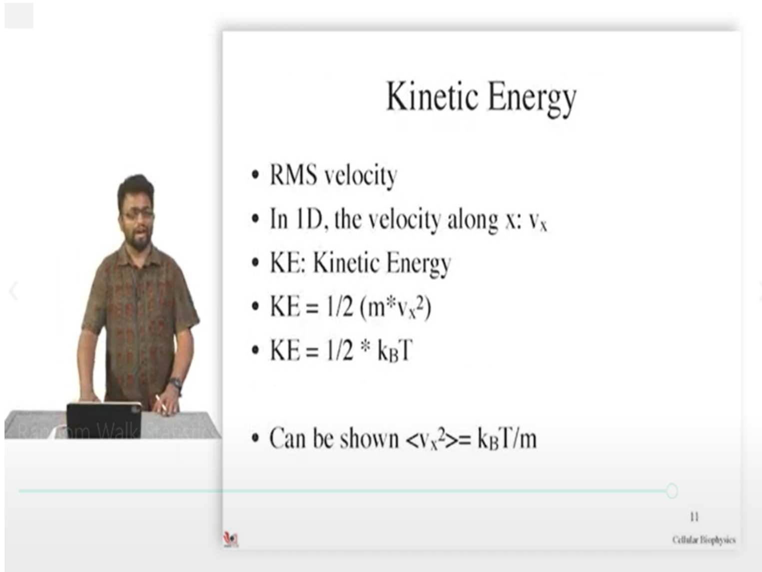

So in order to get an answer to this question we need to infer the RMS root mean square velocity the average velocity that a particle undergoes due to this thermal motion. In one dimension the velocity along x we can call V_x and the kinetic energy KE, So KE from thermodynamics we know in every one any in every direction x y and z is equal to half m v in the case of x x square.

So if you have that and you know that the kinetic energy is half K_B T in one dimension then we can show that V_x square is equal to k_B T or in other words the average root mean square velocity of a particle in one dimension is under root of k_B T by m. k_B T being the thermal energy and m being the mass of the object.

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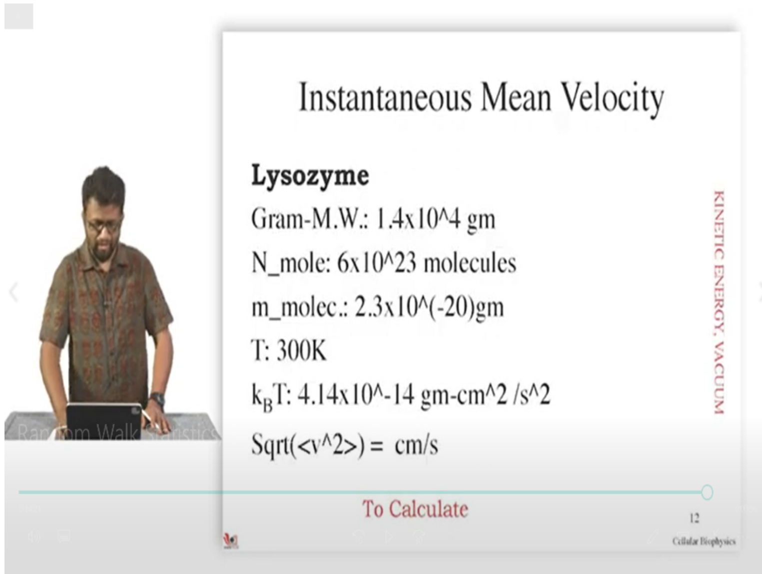

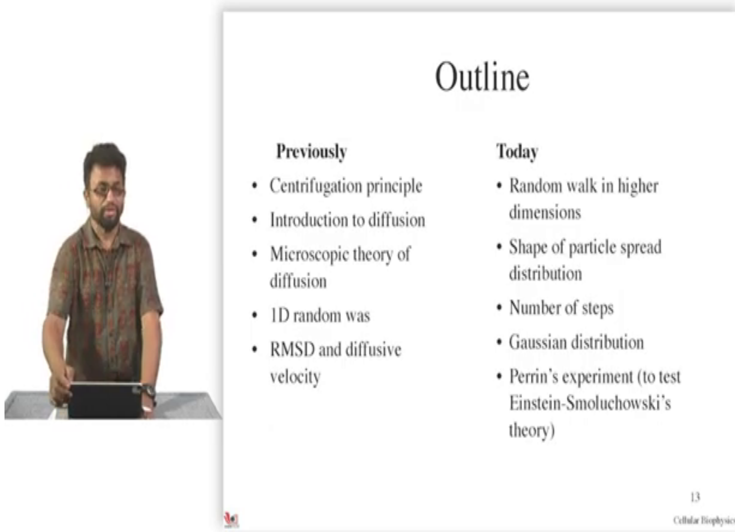

Which means that, we can now calculate this, for example lysozyme, which has a gram molecular weight of 1.4 into 10^4 grams that is 14000 grams. And the number of moles number of molecules in a mole is 6 into 10^{23} that is Avogadro's number. So the molecular mass is 10^{-20} grams with pre-factor 2.3.

And at 300 kelvin when we substitute the values of 4.14 into 10^{-14} grams centimeter square by per second square of k_B T. We get a value which is something I would like to calculate as a part of your exercises.

So for the next steps we are going to talk about random walks in higher dimensions, shape of particle spread distribution, number of steps, Gaussian distribution, Perrin's experiment. Thank you very much.